PTO/SB/21 (08-00) Jease type a plus sign (+) inside this box -> + Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. **Application Number** 09/884,317 TRANSMITTAL **Filing Date** June 19, 2001 **FORM** First Named Inventor Stanley T. Crooke (to be used for all correspondence after initial filing) Group Art Unit 1634 **Examiner Name** A. Chakrabarti otal Number of Pages in This Submission Attorney Docket Number IBIS0038-102/IBIS-0369 ENCLOSURES (check all that apply) After Allowance Communication to Assignment Papers Fee Transmittal Form (for an Application) Group Appeal Communication to Board of Fee Attached Drawing(s) Appeals and Interferences Appeal Communication to Group Amendment / Response Licensing-related Papers (Appeal Notice, Brief, Reply Brief) After Final Petition Proprietary Information Petition to Convert to a Affidavits/declaration(s) ☐ Status Letter Provisional Application Power of Attorney with Revocation Other Enclosure(s) Extension of Time Request and Change of Correspondence (please identify below): Address Terminal Disclaimer Table A Express Abandonment Request Statement Under 37 CFR 3.73(b) Request for Refund with executed Assignment ☐ Information Disclosure Statement CD, Number of CD(s) Certified Copy of Priority Remarks Document(s) Response to Missing Parts/ Incomplete Application Response to Missing Parts under 37 CFR 1.52 or 1.53 SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT Firm

29 DEGENSEAL 2003 CERTIFICATE OF MAILING I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: 29 DELEMBER 2003 Typed or printed name Paul K. Legaard, Registration No. 38,534 Signature Date 29 DECEMBER 2003

Paul K. Legaard, Registration No. 38,534

Individual name

Signature

Date

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be send to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

POWER OF ATTORNEY WITH REVOCATION AND CHANGE OF CORRESPONDENCE ADDRESS

I hereby revoke all previous powers of attorney or authorizations of agent given in the patents/applications identified in Table A attached hereto, and appoint

X Practitioners at Customer Number: 34138 as my/our attorney(s) or agent(s) to prosecute the patents/applications identified in Table A, and to transact all business in the United States Patent and Trademark Office connected therewith. Please change the Correspondence Address for the patent applications identified in Table A to: ▼ Practitioners at Customer Number: 34138 I am the: ☐ Applicant/Inventor. Assignee of record of the entire interest. (A statement under 37 CFR 3.73(b) is enclosed.) Respectfully submitted, ISIS PHARMACEUTICALS, INC. Name: B. Lynne Parshall Title: Executive Vice President



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

STATEMENT UNDER 37 CFR 3.73(b)

Applicant, ISIS Pharmaceuticals, Inc., a corporation, states that it is:

the assignee of the entire right, title, and interest of the patent applications identified in Table A attached hereto.

The extent (by, percentage) of its ownership interest is 100% in the patent applications identified in Table A.

a copy of the pertinent assignment from the inventor(s) of the patent applications identified in Table A is enclosed herewith.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Respectfully submitted,

ISIS PHARMACEUTICALS, INC.

Date: 11-6-03

By://Name: B. Lynne Parshall

Title: Executive Vice President

ASSIGNMENT

WHEREAS, We, Stanley T. Crooke, of Carlsbad, California, Richard Griffey of Vista, California and Steven Hofstadler of Oceanside, California, have invented a certain invention entitled MASS SPECTROMETRIC METHODS FOR BIOMOLECULAR SCREENING, for which we have made application for Letters Patent of the United States, said application having been filed on March 2, 1999 and assigned Application No. 09/260,310; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

DOCKET NO.: IBIS-0013 PATENT

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

DOCKET NO.: IBIS-0013

IN WITNESS WHEREOF, we have hereunto set out hands and seals.

Dated: May 17, 1999

Stanley T. Crooke

State of California
) ss.

County of San Diego

On this 17th day of May, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Stanley T. Crooke) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that the she executed the same in his her authorized capacity,

and that by his per signature on the Assignment the person, or the entity on behalf of which the

CAROL A. COLLINS
Comm. # 1189498
NOTARY PUBLIC - CALIFORNIA
San Diego County
My Comm. Expires July 8, 2002

person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DOCKET NO.: IBIS-0013

PATENT

Dated: MAY 17, 1999, 1999

(Richard Griffey)

State of California)

SS.

County of San Diego

On this ______ day of ______, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Richard Griffey) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he she executed the same in authorized capacity, and that by his her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Coul q. Cell

Signature of Notary

DOCKET NO.: IBIS-0013

PATENT

Dated: MAY 17 1999

(Steven Hofstadler)

State of California

SS.

County of San Diego

On this ______ day of _____ MAy_____, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Steven Hofstadler) personally known t me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Signature of Notary

PATENT DOCKET NO.: IBIS-0013 State of California SS. County of San Diego ____, 1999, before me, the undersigned, a __ day of _ On this _ Notary Public for the state, personally appeared () personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment. WITNESS my hand and official seal. Signature of Notary

Table A

| Serial No. Patent No. Docket No. | Filing Date Issue Date | Inventor(s) | Examiner | Art Unit | Title |
|---|---|------------------------|----------------|----------|---|
| 09/200,355 6,451,524 IBIS0010-100 | November 25, 1998 September 17, 2002 | David J. Ecker | J. Fredman | 1655 | Identification of Disease Predictive Nucleic Acids |
| 09/200,107 6,492,111 IBIS0034-100 | November 25, 1998 December 10, 1998 | David J. Ecker | J. Fredman | 1634 | IN SITU Binary Synthesis of Biologic00ally Effective Molecules |
| 10/209,761 IBIS0034-101 | August 1, 2003 | David J. Ecker | To Be Assigned | 1634 | IN SITU Binary Synthesis of Biologically Effective Molecules |
| 09/076,440 6,221,587 IBIS0035-100 | May 12, 1998 April 24, 2001 | David J. Ecker et al. | E. Campbell | 1656 | Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery |
| 09/310,667 IBIS0035-101 | May 12, 1999 | David J. Ecker et al. | F. Lu | 1634 | Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery |
| 09/076,405 IBIS0036-100 | May 12, 1998 | Richard Griffey et al. | S. Broda | 2123 | Generation of Virtual Combinatorial Libraries of Compounds |
| 09/753,869 IBIS0036-101 | January 3, 2001 | Richard Griffey et al. | M. Borin | 1631 | Generation of Virtual Combinatorial Libraries of Compounds |
| 09/076,447 IBIS0037-100 | May 12, 1998 | Richard Griffey et al. | J. Fredman | 1655 | Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor |

| 00/040 050 | 4000 | | | | |
|---|------------------------------------|---------------------------|------------------|-------------------|---|
| 09/310,653 IBIS0037-101 | May 12, 1999 | Richard Griffey et al. | J. Fredman | 1637 | Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor |
| 09/076,206 6,428,956 IBIS0038-100 | May 12, 1998 August 6, 2001 | Stanley T. Crooke et al. | S. Zitomer | 1634 | Mass Spectrometric Methods for Biomolecular Screening |
| 09/260,310 6,329,146 IBIS0038-101 | March 2, 1999 December 11, 2001 | Stanley T. Crooke | S. Zitomer | 1634 | Mass Spectrometric Methods for Biomolecular Screening |
| 09/884,317 IBIS0038-102 | June 19, 2001 | Stanley T. Crooke | A. Chakrabarti | 1634 | Mass Spectrometric Methods for Biomolecular Screening |
| 09/884,317 IBIS0038-103 | June 27, 2003 | Stanley T. Crooke | To Be Determined | | Mass Spectrometric Methods for Biomolecular Screening |
| 09/076,214 IBIS0039-100 | May 12, 1998 | Richard H. Griffey et al. | T. Friend | 1639 | Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds |
| 09/400,150 IBIS0039-101 | September 21, 1999 | Richard H. Griffey et al. | M. Tran | 1639 | Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds |
| 60/085,092 IBIS0040-001 | May 12, 1998 | Stanley T. Crooke | Not applicable | Not applicable | Small Molecule Targeting Of RNA Structures |
| 09/076,404 IBIS0040-100 | May 12, 1998 | David J. Ecker et al. | A. Marschel | 1631 | Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery |
| 09/310,735 IBIS0040-101 | May 12, 1999 | David J. Ecker et al. | A. Marschel | 1631 | Modulation of Molecular Interaction Sites on RNA and Other Biomolecules |

| 10/104,949 IBIS0040-102 | March 22, 2002 | David J. Ecker et al. | A. Marschel | 1631 | Modulation of Molecular Interaction Sites on RNA and Other Biomolecules |
|----------------------------|-----------------|-----------------------|----------------|-------------------|--|
| 09/310,907 IBIS0041-100 | May 12, 1999 | David J. Ecker et al. | A. Marschel | 1631 | Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same |
| 10/135,017 IBIS0041-101 | April 24, 2002 | David J. Ecker et al. | A. Marschel | 1631 | Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same |
| 09/310,761 IBIS0042-100 | May 12, 1999 | David J. Ecker et al. | M. Schmidt | 1635 | Molecular Interaction Sites of Ornithine Decarboxylase RNA and Methods of Modulating the Same |
| 60/314,236 IBIS0043-001 | August 22, 2001 | David J. Ecker | Not Applicable | Not Applicable | Molecular Interaction Sites of Hepatitis C Virus RNA and Methods of Modulating the Same |
| 10/225,501 IBIS0043-100 | August 19, 2002 | David J. Ecker | To Be Assigned | 1645 | Methods for Identifying Ligand Binding Sites in a Biomolecule |
| 60/314,251 IBIS0044-001 | August 22, 2001 | David J. Ecker | Not Applicable | Not Applicable | Molecular Interaction Sites of 23S Ribosomal RNA and Methods of Modulating the Same |
| 10/224,836 IBIS0044-100 | August 20, 2002 | David J. Ecker | To Be Assigned | 1645 | Molecular Interaction Sites in 23S Ribosomal RNA and Methods of Modulating the Same |
| 60/314,020 IBIS0045-001 | August 21, 2001 | David J. Ecker | Not Applicable | Not Applicable | Molecular Interaction Sites of RNAse P RNA and Methods of Modulating the Same |

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| Multi-Paradigm Knowledge- Bases | Not Applicable | Not Applicable | John McNeil | May 16, 2001 | 60/291,459 IBIS0052-001 |
| Amine Compounds and Combinatorial Libraries Comprising Same | 1627 | T. Prosthofer | Eric Edward Swayze et al. | September 5, 1997 | 08/924,851 IBIS0051-100 |
| Antimicrobial Biaryl Compounds | 1624 | B. Coleman | Elizabeth Jefferson | August 1, 2000 | 09/630,122 IBIS0050-100 |
| Optimization of Ligand Affinity For RNA Targets Using Mass Spectrometry | To Be Assigned | To Be Assigned | Richard H. Griffey et al. | May 16, 2000 | 09/573,479 IBIS0048-101 |
| Optimization Of Ligand Affinity For RNA Targets Using Mass Spectrometry | To Be Assigned | To Be Assigned | Richard H. Griffey et.al. | February 8, 2000 | 09/499,875 IBIS0048-100 |
| Methods for Identifying Ligand Binding Sites in a Biomolecule | 1645 | To Be Assigned | Richard H. Griffey et al. | July 31, 2002 | 10/209,692 IBIS0047-101 |
| Methods for Identifying Ligand Binding Sites in a Biomolecule | 1637 | J. Riley | Richard H. Griffey et al. | February 22, 2001 | 09/791,147 IBIS0047-100 |
| Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same | 1645 | To Be Assigned | David J. Ecker | August 16, 2002 | 10/223,126 IBIS0046-100 |
| Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same | Not Applicable | Not Applicable | David J. Ecker | August 21, 2001 | 60/313,890 IBIS0046-001 |
| Molecular Interaction Sites of RNAse P RNA and Methods of Modulating the Same | 1645 | To Be Assigned | David J. Ecker | August 16, 2002 | 10/223,156 IBIS0045-100 |

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| 10/150,668 IBIS0052-100 | May 16, 2002 | John McNeil et al. | To Be Assigned | 2176 | Multi-Paradigm Knowledge- Bases |
|---|-----------------------------------|--------------------------|-----------------|------|--|
| 09/411,748 6,429,016 IBIS0053-100 | October 1, 1999 August 6, 2002 | John McNeil | Patricia A. Bex | 1743 | System and Method for Sample Positioning in a Robotic System |
| 10/153,327 IBIS0053-101 | May 22, 2002 | John McNeil | To Be Assigned | 1743 | System and Method for Sample Positioning in a Robotic System |
| 10/067,017 IBIS0054-100 | February 24, 2002 | Michael L. Migawa | T. McKenzie | 1624 | Novel Pyranosyl Cytosines: Pharmaceutical Formulation and Methods |
| 10/071,978 IBIS0055-100 | February 6, 2002 | Eric E. Swayze et al. | K. Habte | 1624 | Novel Benzimidazole Compounds |
| 09/678,434 IBIS0056-100 | October 2, 2000 | John McNeil | E. Quan | 1743 | Self-Dispensing Storage Device |
| 09/310,844 IBIS0058-100 | May 12, 1999 | David J. Ecker et al. | M. Schmidt | 1635 | Molecular Interaction Sites of Interleukin-2 RNA and Methods of Modulating the Same |
| 09/499,875 IBIS0059-100 | February 8, 2000 | Richard Griffey et al. | M. Tran | 1639 | Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry |
| 09/573,479 IBIS0059-101 | May 16, 2000 | Richard Griffey et al. | T. Prosthofer | 1627 | Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry |
| 10/005,344 ISIS0052-100 | December 4, 2001 | Loren J. Miraglia et al. | T. Gibbs | 1635 | Antisense Modulation of Human MDM2 Expression |

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|---|---|--|---|
| • | Oligoribonucleotides and Ribonucleases for Cleaving RNA | Antisense Modulation of SMAD6 Expression | |
| | 1635 | 1635 | |
| | To Be Assigned | To Be Assigned | |
| | Stanley T. Crooke | Brett P. Monia et al. | |
| | October 25, 2002 | December 20, 2002 | |
| | 10/281,349 ISIS0002-105 | 10/327,805 ISIS0060-101 | |